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(54) Title: IMPROVED ELECTROPHYSIOLOGICAL ASSAYS USING OOCYTES THAT EXPRESS HUMAN ENaC AND THE  
USE OF PHENAMIL TO IMPROVE THE EFFECT OF ENaC ENHANCERS IN ASSAYS USING MEMBRANE POTENTIAL  
REPORTING DYES

(57) Abstract: In one aspect, the present invention relates to a mammalian cell-based high-throughput assay for the profiling and  
screening of human epithelial sodium channel (hENaC) cloned from a human kidney c-DNA library and is also expressed in other  
tissues including human taste tissue. The present invention further relates to amphibian oocyte-based medium-throughput elec-  
trophysiological assays for identifying human ENaC modulators, preferably ENaC enhancers. Compounds that modulate ENaC  
function in a cell-based ENaC assay are expected to affect salty taste in humans. The assays described herein have advantages over  
existing cellular expression systems. In the case of mammalian cells, such assays can be run in standard 96 or 384 well culture  
plates in high-throughput mode with enhanced assay results being achieved by the use of a compound that inhibits ENaC function,  
preferably an amiloride derivative such as Phenamil. In the case of the inventive oocyte electrophysiological assays (two-electrode  
voltage-clamp technique), these assays facilitate the identification of compounds which specifically modulate human ENaC. The  
assays of the invention provide a robust screen useful to detect compounds that facilitate (enhance) or inhibit hENaC function. Com-  
pounds that enhance or block human ENaC channel activity should thereby modulate salty taste in humans.

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